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Doctor Robert C. Hockett
Associate Scientific Director
The Council for Tobacco Research - U.S.A.
633 Third Avenue
New York, New York 10017

Dear Dr. Hockett:-

It was indeed a pleasure to receive Drs. Lisanti's, Little's and your memorandum of Nov. 24, 1965 re: "Impressions and Recommendations of Conference Role of Oral Cavity Research in the Study of Tobacco Use and Human Health" and to see the extent to which you relied upon and adapted my comments and recommendations into your own.

My prime purpose for writing this letter is prompted by some unexpected, yet exceedingly promising findings which have emerged from a tangential, but pertinent line of approach to our main line of attack concerning "Metabolic Interrelationships Between Tobacco Smoke and the Human Mouth", Project #Q203.

Recently, one of our colleagues developed a new gas-liquid chromatographic assay method for the detection and quantitation of carbonyls (organic ketones and aldehydes) which, to our knowledge, is unique in the sense of its greatly increased sensitivity compared to otherwise available methods and its consequent ease of application to biological systems. This assay method has been applied to the analysis of easily obtained human saliva samples of a non-smoker and heavy cigar smoker.

Time of retention curves are shown in the accompanying graph. Curve (II) gives a spectrum of compounds found in the saliva of the non-smoker harvested immediately upon arising after a full nights sleep but prior to eating, drinking, rinsing or brushing of the teeth. Over the course of the experiment some 29 unidentified components are evident suggesting at least 29 substances, most of which undoubtedly have not been described in human saliva before, and some of which may not have been described in human fluids or, for that matter, biological samples of any kind before.

Curve (III) gives a spectrum of compounds for a comparable sample of saliva obtained from the same non-smoker the following morning immediately upon awakening, but after smoking (without inhaling) 4 cigarettes

(Winston). It is evident from the retention time 0 to 10 minutes that a great deal of one, two or three carbon carbonyl compounds are trapped in the saliva, component 1. In addition, three new components - 2, 3 and 4, not present in the saliva without smoking, also are trapped and appear in the saliva after smoking. From their retention times, 27.2 minutes, 33.6 minutes, and 40.1 minutes, these components are either lower molecular weight hydroxy carbonyls or carbonyl compounds of eleven or more carbon atoms. The many components (5 to 17) in the non-smoker's saliva sample without or after smoking, retention time 6.1 minutes to 31.0 minutes, represent a possible host of three to eleven carbon carbonyl compounds apparently unrelated to tobacco smoke. In addition two very long retention time carbonyls, about 50.0 minutes and 57.0 minutes, also are normally present in saliva, components 18 and 19, respectively.

Curve (I) shows the spectrum of compounds found in a comparable saliva collected from an habitual cigar smoker upon awakening in the morning after a full night's sleep, but before eating, drinking, rinsing, brushing of teeth or smoking. Much of the detail, over the range of 6 to 31 minutes found in the saliva of the non-smoker, appears to be absent in that of the habitual smoker. The particularly large peaks, possibly components 18 and 19, may be the result of using a still newer isolation technique designed to recover components of low volatility in larger quantity. It is anticipated that future collections of saliva from the non-smoker might show intensification of peaks. In addition, although the analytical method employed here has been established as quantitative, optimum column conditions must be realized for separation of these components. Such improvement would naturally result in precise retention times and lead to identification of the components.

These results and emerging perspective suggest that bio=assays or tests relating to the tobacco smoking habit may become a reality. In addition, identification of these compounds could lead to definitive experiments aimed at establishing essential metabolic interrelationships between tobacco, tobacco smoke products and the human oral cavity or other biological systems of concern.

Several practical factors, mostly economic however, are operating which work against this probable breakthrough becoming an effective one. The equipment which is required for this new and novel situation is quite expensive. Before large sums of money are requested, we believe it would be most wise to pursue a feasibility study to verify and extend the initial findings. Thus far we have been using and are continuing to use part of the funds granted under Project #Q203 to defray current costs. The advantage here is that we have use of the necessary equipment at the present time on an interim basis at low cost. Unfortunately this advance expenditure of funds is a luxury that the limited budget available under Q203 can ill afford.

Consequently, I am taking the liberty to make this informal report a letter of request for the sum of two thousand and five hundred dollars ($2,500.00) to complete a quick feasibility study along these lines within the next 45 to 50 days. Then if the results continue on their promising way and provide ample

justification, we will submit a formal proposal for the March 1966 meeting of the CTR - U.S.A. to cover equipping the necessary laboratory, salaries etc. for the full development, exploitation and program integration of this approach.

In the meantime our metabolic studies under Q203 are in progress.

Wishing you, Drs. Little and Brady a very Merry Christmas and most Happy New Year, I remain,

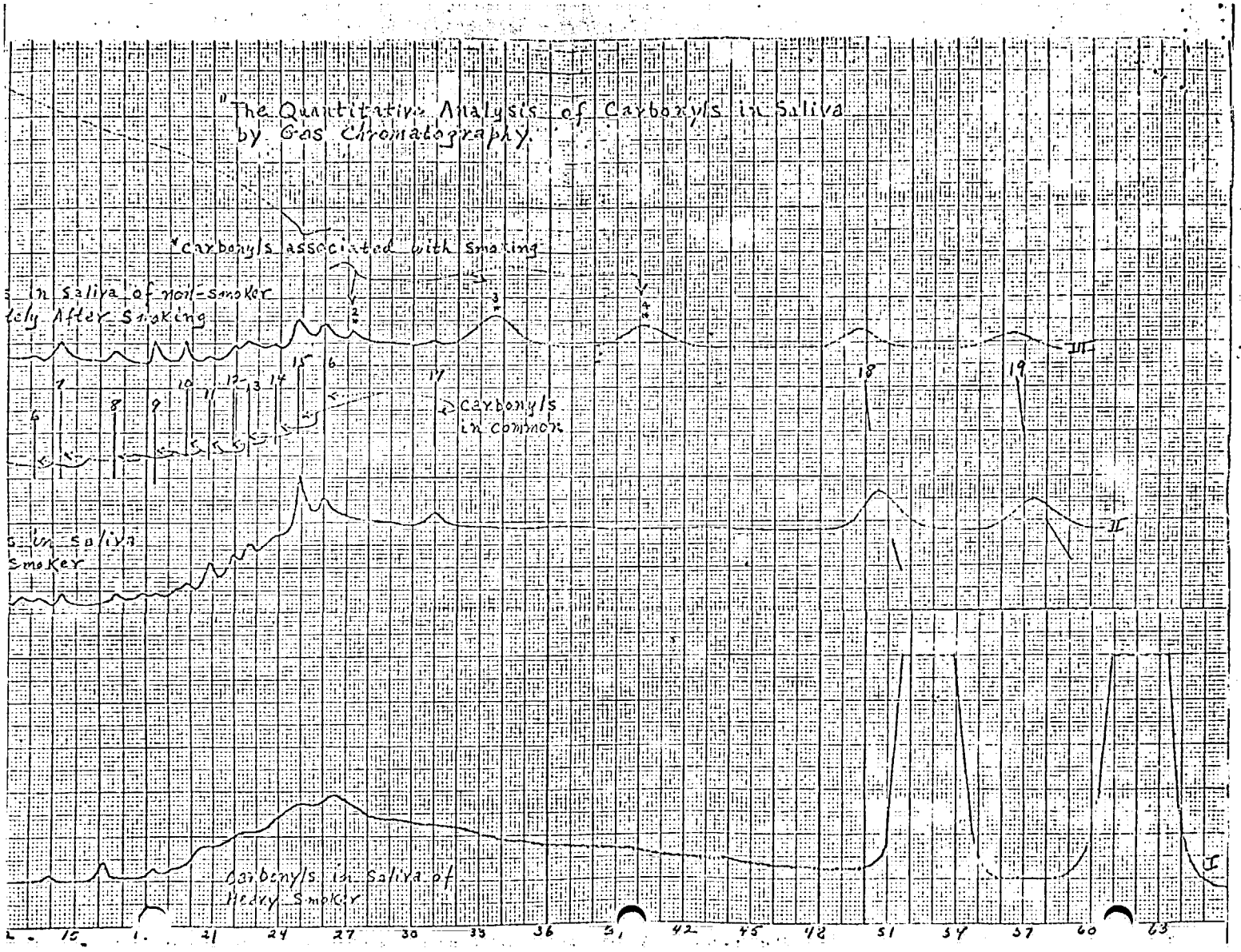
Sincerely yours,

Bertram Eichel

Bertram Eichel, D.D.S.
Director

BE/md

encl. (Graph)



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